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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,752	11/21/2001	Darja Fercej Temeljotov	033248-017	5309

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,752	FERCEJ TEMELJOTOV ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-18,20-30 and 34-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18,20-30 and 34-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Request for Continued Examination and Amendments/Remarks filed 1/3/06 is acknowledged. Claims **16-18, 20-30, 34-60** are pending in this application.

Response to Arguments

Applicant's arguments with respect to claims have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-21, 30, 34, 38-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 16 is directed to a composition comprising clarithromycin; 10-36% of fatty component selected from behenic acid, glycerol behenate, or a mixture thereof; and 5-18% of a hydrophilic component selected from xanthan gum, guar gum, acacia, or a mixture.

Dependent claim 20 recites "wherein *the* hydrophilic component comprises hydroxypropyl methylcellulose" which is vague and indefinite since the parent claim defines "the hydrophilic component" as xanthan gum, guar gum, acacia, or a mixture thereof. The examiner suggests applicant amend the claim to "the pharmaceutical composition according to claim 16 further comprising hydroxypropyl methylcellulose...".

Independent claim 27 is directed to a process of making a composition comprising

clarithromycin; 10-36 of a fatty component selected from behenic acid, glycerol behenate, or a mixture thereof; and 5-18% of a hydrophilic component selected from xanthan gum, guar gum, acacia, or a mixture thereof.

Dependent claim 30 recites "wherein *the* fatty component comprises is selected from triglycerides of higher saturated fatty acids, hydrogenated oils, and mixtures thereof", which is vague and indefinite since the parent claim defines "the fatty component" as behenic acid, glycerol behenate, or a mixture thereof.

Claim 34 depends on a cancelled claim and thus the dependency of claim 34 is indefinite.

Independent claim 35 is directed to a composition comprising clarithromycin; 10-36% glycerol behenate; and 5-18% hydroxypropylmethylcellulose.

Dependent claim 38 recites the limitation "the hydrophilic component" in line 2. There is insufficient antecedent basis for this limitation in the claim. The examiner suggests amending the claim to "wherein the hydroxypropylmethylcellulose has a low viscosity".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 45, 50-52 are under 35 U.S.C. 102(b) as being anticipated by WO 95/22319 to Briskin et al.

Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5% povidone, 26% carbopol, 5% hydroxypropyl cellulose (an alkyl-substituted cellulose ether), 10% glyceryl

behenate, and 10% microcrystalline cellulose. See table 1 on page 8. The composition is then formulated in to a tablet or capsule. See page 7, line 7. On page 6, the method of making the tablet is disclosed wherein the particles are sieved, dry blended and compressed to form a tablet. Briskin discloses on page 5, lines 34-35 an enteric coating. Note that enteric coating is inherently acid resistant coating.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 16-17, 22, 24-30, 34-36, 40, 42-44, 46, 48, 53-54, 56, 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5,811,120).

Briskin teaches a process for the preparation of the fine particle pharmaceutical formulations comprises a) adding to the dry components of the formulation an extrusion aid

material, wherein the extrusion aid material is selected from pharmaceutically acceptable oils and waxes having a drop point ranging between about 15.degree. C. and 115.degree. C.; b) thoroughly blending the dry mixture; c) wetting the mixture resulting from step b) to form a granular mixture of the formulation; d) extruding the granular mixture through a mesh; e) spheronizing the extrudate; and f) drying the fine particles resulting from step e) to form a fine particle formulation. See page 2, lines 8-16.

Briskin teaches the most preferred extrusion aid materials include a hydrogenated vegetable oil (Lubritab) and glyceryl behenate (Compritol). Preferably, the extrusion aid material is present in the formulations made by the process of this invention in amounts ranging between about 1-75%. See page 4, lines 30-35 to page 5, lines 1-2. The formulation contains ingredients in addition to the active therapeutic agent and the extrusion aid material, which are chosen to tailor the final formulation for its intended purpose. For instance, for a rapidly dissolving drugs, conventional binding agents may be added to the formulations to retard too-rapid dissolution. Suitable binder agents include polyvinylpyrrolidone (such as Povidone) and carboxymethyl celluloses, and hydroxymethylcelluloses. The examples utilize HMC in an amount of 5%.

Specifically, Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5% povidone (binding agent), 26% carbopol, 5% hydroxypropyl cellulose (binding agent), 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8. the composition is then formulated in to a tablet or capsule. See page 7, line 7. The total amount of the binding agent is 10.5% in example 1b. On page 6, the method of making the tablet is disclosed wherein the particles are sieved, dry blended and compressed to form a tablet. Briskin

discloses on page 5, lines 34-35 an enteric coating. Note that enteric coating is inherently acid resistant coating.

With regard to independent claim 16 and 27, although Briskin teaches the use of hydrophilic binders, Briskin does not teach the instant hydrophilic component (xanthan gum, guar gum, or acacia). With regard 33, although Briskin teaches the use of HMC as the hydrophilic binder, Briskin does not the use of hydroxypropylmethylcellulose (HPMC). Further, Briskin does not teach instant surfactant.

Gibson et al teach pharmaceutical formulations containing raloxifene. Gibson et al teaches the conventional additives in pharmaceutical formulations such as hydrophilic binders. Gibson teaches the term "hydrophilic binder" represents binders *commonly used in the formulation of pharmaceuticals*, such as polyvinylpyrrolidone, polyethylene glycol, sucrose, dextrose, corn syrup, polysaccharides (including acacia, tragacanth, guar, and alginates), gelatin, and cellulose derivatives (including hydroxypropyl methylcellulose, hydroxypropyl cellulose, and sodium carboxymethylcellulose). See column 3, lines 50-60. Further, Gibson teaches the use of surfactants including sodium docosate and lubricants including glyceryl behenate. See column 3, lines 60-67. Further, the reference teaches that the preparation of the oral formulations is well known in the art such as direct compression. The process includes mixing the active with the hydrophilic binder and surfactant, which is then, milled if necessary, drying the granules, and compressing into tablets (col. 5, lines 10-15).

It would have been obvious of one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin et al and Gibson et al and utilize the hydrophilic binder. With regard to claim 16 and 27, one would have been motivated to substitute Briskin's

cellulose derivative (HMC) with the instant hydrophilic binder acacia or guar gum with the expectation of similar results since Gibson teaches that both Briskin's hydrophilic binder and instant hydrophilic binders are conventional hydrophilic binders utilized routinely in pharmaceutical compositions. Therefore, it is prima facie obvious for a skilled to substitute one functional equivalent with another known functional equivalent with the expectation of similar results and success since the art establishes that both are hydrophilic and act as binders in the composition.

With regard to claim 33, it would have been motivated to substitute Briskin's cellulose derivative (HMC) for instant cellulose derivative (HPMC) with the expectation of similar results since Gibson teaches that both are conventional hydrophilic binders utilized in pharmaceutical compositions. Therefore, it is prima facie obvious for a skilled artisan to substitute one functional equivalent with another known functional equivalent with the expectation of similar results and success since the art establishes that both are hydrophilic and act as binders in the composition.

Additionally, Gibson teaches the conventional use of surfactants such as instant sodium docusate in pharmaceutical compositions. Thus, the use of conventional additives in the preparation of pharmaceuticals is prima facie obvious.

Note that since the prior art teaches the instant ratio of claim 29 and the prior art's composition is structurally similar in that the weight percent of the hydrophilic component and hydrophobic component are the same; thus the two compositions will behave in the same manner.

Claims 20-21 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5,811,120) in further view of Evenstad et al (5,126,145).

The teachings of Briskin and Gibson have been set forth above. Briskin teaches the use of HPC as the hydrophilic *binder* and Gibson teaches the use of HPC or HPMC as the hydrophilic *binder*.

The references do not specify the viscosity of HPMC.

Evenstad teaches a controlled release tablet. Evenstad teaches the use of high viscosity HPMC to provide sustain release whereas a water-soluble pharmaceutical binder such as HPMC having binding properties has a much lower viscosity; typically a viscosity of less than 100 cps such as METHOCEL E15. See column 3, lines 5-67. METHOCEL E15 has a viscosity of 12-18 cps.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin, Gibson, and Evenstad and specifically utilize a low viscosity HPMC. One would have been motivated to do so since Evenstad teaches high viscosity HPMC is useful for its sustaining action and low viscosity HPMC is useful for its binding properties. Therefore, a skilled artisan would have been motivated to utilize a low viscosity HPMC with the expectation of similar results since both Briskin and Gibson teach the use of the cellulose derivative for its binding property and Evenstad teaches the low viscosity cellulose derivative provide this function.

Claims 47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view Curatolo et al (5,605,889).

The teaching of Briskin has been set forth above.

Although, Briskin teaches the use of conventional excipients in the composition, Briskin does not teach the use of the instant phosphate buffer.

Curatolo teaches azithromycin compositions. Curatolo teaches in addition to the active ingredient azithromycin, the tablets may be formulated with a variety of *conventional excipients* such as binders, flavorings, buffers, diluents, colors, lubricants, sweetening agents, thickening agents, and glidants. See column 6, lines 55-66. Curatolo teaches a powder composition used to make suspensions may also contain conventional optional ingredients such as a buffer to maintain a high pH upon reconstitution. Suitable buffers and pH-altering agents include anhydrous tribasic sodium phosphate, anhydrous sodium carbonate, glycine, and the like. See column 8, line 60 to column 9, line 2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin and Curatolo and utilize conventional excipients such as buffers. One would have been motivated to do so since the use of conventional additives such as buffers are routinely utilized in the art for maintaining the pH of a composition as taught by Curatolo. Thus, a skilled artisan would have been motivated to utilize a buffer to maintain the desired pH of the composition.

Claims 18, 23, 37, 41, 55, 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5811120) in further view of Curatolo et al (5,605,889).

The teachings of Briskin and Gibson have been set forth above.

Although, Briskin teaches the use of conventional excipients in the composition, Briskin does not teach the use of the instant phosphate buffer.

Curatolo teaches azithromycin compositions. Curatolo teaches in addition to the active ingredient azithromycin, the tablets may be formulated with a variety of *conventional excipients* such as binders, flavorings, buffers, diluents, colors, lubricants, sweetening agents, thickening agents, and glidants. See column 6, lines 55-66. Curatolo teaches a powder composition used to make suspensions may also contain conventional optional ingredients such as a buffer to maintain a high pH upon reconstitution. Suitable buffers and pH-altering agents include anhydrous tribasic sodium phosphate, anhydrous sodium carbonate, glycine, and the like. See column 8, line 60 to column 9, line 2.

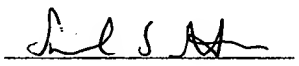
It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin, Gibson, and Curatolo and utilize conventional excipients such as buffers. One would have been motivated to do so since the use of conventional additives such as buffers are routinely utilized in the art for maintaining the pH of a composition as taught by Curatolo. Thus, a skilled artisan would have been motivated to utilize a buffer to maintain the desired pH of the composition.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sharmila S. Gollamudi
Examiner
Art Unit 1616